

PATENT APPLICATION SERIAL NO. 10/521175

U.S. DEPARTMENT OF COMMERCE  
PATENT AND TRADEMARK OFFICE  
FEE RECORD SHEET

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01 FC:1631	300.00 OP -
02 FC:1632	500.00 OP -
03 FC:1633	200.00 OP -
04 FC:1601	250.00 OP -
05 FC:1615	700.00 OP -

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02 FC:1616	260.00 DA	100.00 OP

02 FC:1632

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Adjustment date: 09/22/2006 THOLLAND  
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02 FC:1616 260.00 CR -100.00 OP

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DA#: 230975 Name/Number: 10521175  
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COMPLETED  
PCT NATIONAL DIVISION



DEP & REF

PATENT MAINTENANCE  
IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Is an application of

Shouji KAMIYA et al.

Serial No. 10/521,175

Filed March 14, 2005

NOVEL INDOLINE COMPOUND AND MEDICINAL USE THEREOF

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US PATENT & TRADEMARK  
OFFICE

ACCOUNTING DIVISION  
REFUND BRANCH

: Attorney Docket No. 2005\_0042A  
Confirmation No. 2857

REQUEST FOR REFUND

Commissioner for Patents  
P.O. Box 1450  
Alexandria, VA 22313-1450

REFUND COMPLETED  
PCT NATIONAL DIVISION

Sir:

Applicants respectfully request a refund of \$260.00 charged to Deposit Account No. 23-0975 on August 15, 2005. The fee code indicates the charge is for multiple dependent claims and the applicants assert this is incorrect.

Applicants' attorney submitted a Preliminary Amendment on January 15, 2005 at the time of filing. The Amendment deleted all multiple dependencies in order to reduce the filing fee and eliminate any improper claims. A copy is enclosed for reference.

Kindly credit the refund of \$260.00 to the deposit account of undersigned, no. 23-0975. If there are any questions regarding this matter, please contact Kara Reade, Accounting Assistant, at (202) 721-8226.

Respectfully submitted,

Shouji KAMIYA et al.

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March 10, 2006

09/22/2006 THAILAND 10521175  
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260.00 CR -120.00 CR

2005\_0042A



IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of

Shouji KAMIYA et al.

Serial No. NEW

Filed January 14, 2005

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**Mail Stop: PCT**

**Attorney Docket No. 2005\_0042A**

NOVEL INDOLINE COMPOUND AND MEDICINAL  
USE THEREOF

**[Corresponding to PCT/JP03/09012**

**Filed July 16, 2003]**

**PRELIMINARY AMENDMENT**

Commissioner for Patents  
P.O. Box 1450  
Alexandria, VA 22313-1450

Sir:

**Prior to calculating the filing fee**, please amend the above-identified application as follows:

ATTACHMENT D

### Amendments to the Specification

**Page 1, immediately after the title, please insert:**

This application is a U.S. national stage of International Application No. PCT/JP03/09012 filed July 16, 2003.

**Page 16, line 2, after the formulas to page 17, line 3, please rewrite as follows:**

wherein R<sup>1</sup>, R<sup>3</sup> and R<sup>5</sup> are each as defined above, R<sup>4a</sup> is alkyl group, cycloalkyl group, cycloalkylalkyl group or lower alkoxy lower alkyl group, R<sup>8</sup> is amino protecting group, R<sup>9</sup> is alkyl group or aryl group, R<sup>12a</sup> is hydrogen atom, lower alkyl group or lower alkoxy lower alkyl group and X is a leaving group such as halogen atom (chlorine atom, bromine atom or iodine atom), alkanesulfonyloxy (e.g., methanesulfonyloxy, ~~ethanesulfonisoxy~~ ethanesulfonyloxy, propanesulfonyloxy or trifluoromethanesulfonyloxy etc.) or arylsulfonyloxy (e.g., phenylsulfonyloxy or tolylsulfonyloxy etc.) and the like.

**Page 19, lines 4-15, please rewrite as follows:**

The compound (V) is used for this reaction as a free carboxylic acid, or as a reactive derivative thereof, and both embodiments are encompassed in this reaction. To be specific, it is subjected to this reaction as a free acid or a salt with a base such as sodium, potassium, calcium, triethylamine, pyridine and the like, or a reactive derivative thereof such as an acid halide (acid chloride, acid bromide etc.), an acid anhydride, a mixed acid anhydride [a mixed acid anhydride with substituted phosphoric acid (dialkylphosphoric acid etc.), an alkyl carbonate (monoethyl carbonate etc.) and the like], an active amide (amide with imidazole and the like), an ester (cyanomethyl ester, 4-nitrophenyl ester etc.) and the like.

**Page 32, line 9 to page 33, line 8, please rewrite as follows:**

As the hydroxy protecting group for R<sup>14</sup>, for example, a group capable of forming ethers and acetals acetals, such as methyl ether, isopropyl ether, tert-butyl ether, benzyl ether, allyl

ether, methoxymethyl ether, tetrahydropyranyl ether, p-bromophenacyl ether, trimethylsilyl ether and the like; like, a group capable of forming esters, esters such as formyl, acetyl, monochloroacetyl, dichloroacetyl, trifluoroacetyl, methoxycarbonyl, ethoxycarbonyl, benzyloxycarbonyl, p-nitrobenzyloxycarbonyl, 2,2,2-trichloroethoxycarbonyl, benzoyl, methanesulfonyl, benzenesulfonyl, p-toluenesulfonyl and the like, and the like can be mentioned.

**Page 39, lines 12-20, please write as follows:**

(6) The compound (0.8 g) obtained in (5) was dissolved in methanol (8 mL) and 4M aqueous sodium hydroxide solution (3 mL) was added. The mixture was stirred at 80°C for 15 min. The solvent was evaporated under reduced pressure and the obtained residue was dissolved in chloroform (50 mL). The solution was washed successively with water and saturated brine and dried over sodium sulfate. Chloroform was evaporated under reduced pressure and the The obtained residue was purified by silica gel column chromatography to give N-(4,6-dimethyl-5-nitroindolin-7-yl)-2,2-dimethylpropanamide (0.68 g).

**Page 39, line 25 to page 40, line 1, please rewrite as follows:**

(7) The compound (3.5 g) obtained in (6) was dissolved in N,N-dimethylformamide (40 mL) and sodium hydride (60% oil suspension) (576 mg) was added in portions under a nitrogen atmosphere and under ice-cooling. After stirring at room temperature for 10 min, octyl iodide (2.6 mL) was added and the mixture was at the same temperature for 17 hr. Water (100 mL) was added and the mixture was extracted with diethyl ether (300 mL). The diethyl ether layer was washed successively with water and saturated brine and dried over sodium sulfate. Diethyl ether was evaporated under reduced pressure and the The obtained residue was purified by silica gel column chromatography to give the title compound as crystals (3.2 g).

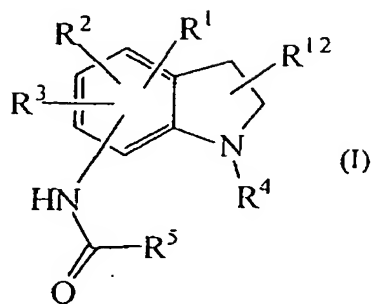
Page 65, lines 6-24, please rewrite as follows:

(5) The compound (5.9 g) obtained in (4) was dissolved in methanol (185 mL), and 5% palladium-carbon (1.78 g) was added. The mixture was subjected to catalytic hydrogenation at 35°C, 3 kgf/cm<sup>2</sup> for 16 hr. Palladium-carbon was filtered off, and the solvent was evaporated under reduced pressure. Ethyl acetate (50 mL) was added to the obtained crystalline residue and the crystals were washed by stirring the mixture and collected by filtration to give ~~1-acetyl-2-methoxymethyl-4,6-dimethylindoline~~ 1-acetyl-7-amino-2-methoxymethyl-4,6-dimethylindoline hydrobromide as crystals (4.95 g). The obtained crystals were dissolved in methylene chloride (50 mL), and pivaloyl chloride (1.94 mL) was added and triethylamine (4.4 mL) was added dropwise under ice-cooling. The mixture was stirred at the same temperature for 1 hr, and the reaction mixture was washed successively with 5% aqueous citric acid, water and saturated brine (each 50 mL) and dried over sodium sulfate. Methylene chloride was evaporated under reduced pressure and the obtained residue was purified by silica gel column chromatography to give N-(1-acetyl-2-methoxymethyl-4,6-dimethylindolin-7-yl)-2,2-dimethylpropanamide (4.87 g).

## Amendments to the Claims

### 1. (Original)

A novel indoline compound represented by the formula (I)



wherein

$R^1$  and  $R^3$

are the same or different and each is hydrogen atom, lower alkyl group or lower alkoxy group,

$R^2$  is  $-\text{NO}_2$ ,  $-\text{NHSO}_2\text{R}^6$  [ $\text{R}^6$  is alkyl group, aryl group or  $-\text{NHR}^7$  ( $\text{R}^7$  is hydrogen atom,  $-\text{COR}^{13}$  ( $\text{R}^{13}$  is hydrogen atom or lower alkyl group) or lower alkoxy carbonyl group)],  $-\text{NHCONH}_2$  or lower alkyl group substituted by  $-\text{NHSO}_2\text{R}^6$  [ $\text{R}^6$  is alkyl group, aryl group or  $-\text{NHR}^7$  ( $\text{R}^7$  is hydrogen atom,  $-\text{COR}^{13}$  ( $\text{R}^{13}$  is hydrogen atom or lower alkyl group) or lower alkoxy carbonyl group)],

$R^4$  is hydrogen atom, alkyl group optionally substituted by hydroxy group,  $-\text{COR}^{13}$  ( $\text{R}^{13}$  is hydrogen atom or lower alkyl group), lower alkenyl group, lower alkoxy lower alkyl group, lower alkylthio lower alkyl group, cycloalkyl group or cydoalkylalkyl group,

$R^5$  is alkyl group, cycloalkyl group or aryl group,

$R^{12}$  is hydrogen atom, lower alkyl group, lower alkoxy lower alkyl group or lower alkylthio lower alkyl group,

or a pharmaceutically acceptable salt thereof.

### 2. (Original)

The novel indoline compound of claim 1, wherein, in the formula (I),  $R^1$  and  $R^3$  are the same or different and each is hydrogen atom, lower alkyl group or lower alkoxy

group,  $R^2$  is  $-NO_2$ ,  $-NHSO_2R^6$  [ $R^6$  is alkyl group, aryl group or  $-NHR^7$  ( $R^7$  is hydrogen atom,  $-COR^{13}$  ( $R^{13}$  is hydrogen atom or lower alkyl group) or lower alkoxy carbonyl group)],  $-NHCONH_2$  or lower alkyl group substituted by  $-NHSO_2R^6$  [ $R^6$  is alkyl group, aryl group or  $-NHR^7$  ( $R^7$  is hydrogen atom,  $-COR^{13}$  ( $R^{13}$  is hydrogen atom or lower alkyl group) or lower alkoxy carbonyl group)],  $R^4$  is hydrogen atom, alkyl group, cycloalkyl group or cycloalkylalkyl group,  $R^5$  is alkyl group, cycloalkyl group or aryl group, and  $R^{12}$  is hydrogen atom, or a pharmaceutically acceptable salt thereof.

**3. (Original)** The novel indoline compound of claim 1, wherein, in the formula (I),  $R^2$  is  $-NHSO_2R^6$  [ $R^6$  is alkyl group or  $-NHR^7$  ( $R^7$  is hydrogen atom)],  $R^4$  is alkyl group optionally substituted by hydroxy group,  $-COR^{13}$  ( $R^{13}$  is hydrogen atom or lower alkyl group), lower alkenyl group, lower alkoxy lower alkyl group or lower alkylthio lower alkyl group,  $R^5$  is alkyl group,  $R^{12}$  is hydrogen atom, lower alkyl group, lower alkoxy lower alkyl group or lower alkylthio lower alkyl group, or a pharmaceutically acceptable salt thereof.

**4. (Original)** The novel indoline compound of claim 2, wherein, in the formula (I),  $R^2$  is  $-NHSO_2R^6$  [ $R^6$  is alkyl group or  $-NHR^7$  ( $R^7$  is hydrogen atom)] or  $-NHCONH_2$ , or a pharmaceutically acceptable salt thereof.

**5. (Original)** The novel indoline compound of claim 2, wherein, in the formula (I),  $R^2$  or  $-NHCOR^5$  is bonded to the 5-position of indoline, and the other is bonded to the 7-position of indoline, or a pharmaceutically acceptable salt thereof.

**6. (Original)** The novel indoline compound of claim 3, wherein, in the formula (I),  $R^2$  is bonded to the 5-position of indoline, and  $-NHCOR^5$  is bonded to the 7-position of indoline, or a pharmaceutically acceptable salt thereof.



7. (Original) The novel indoline compound of claim 4, wherein, in the formula (I),  $R^2$  is bonded to the 5-position of indoline, and  $-NHCOR^5$  is bonded to the 7-position of indoline, or a pharmaceutically acceptable salt thereof.
8. (Original) The novel indoline compound of claim 6, wherein, in the formula (I),  $R^4$  is lower alkoxy lower alkyl group or lower alkylthio lower alkyl group, and  $R^{12}$  is hydrogen atom or lower alkyl group, or a pharmaceutically acceptable salt thereof.
9. (Original) The novel indoline compound of claim 8, wherein, in the formula (I),  $R^1$  and  $R^3$  are lower alkyl groups, or a pharmaceutically acceptable salt thereof.
10. (Original) The novel indoline compound of claim 6, wherein, in the formula (I),  $R^{12}$  is bonded to the 2-position of indoline, or a pharmaceutically acceptable salt thereof.
11. (Original) The novel indoline compound of claim 10, wherein, in the formula (I),  $R^4$  is alkyl group,  $R^{12}$  is lower alkoxy lower alkyl group or lower alkylthio lower alkyl group, or a pharmaceutically acceptable salt thereof.
12. (Original) The novel indoline compound of claim 11, wherein, in the formula (I),  $R^1$  and  $R^3$  are lower alkyl groups, or a pharmaceutically acceptable salt thereof.
13. (Original) The novel indoline compound of claim 7, wherein, in the formula (I),  $R^1$  and  $R^3$  are lower alkyl groups, and  $R^5$  is alkyl group, or a pharmaceutically acceptable salt thereof.
14. (Original) The novel indoline compound of claim 13, wherein, in the formula (I),  $R^2$  is  $-NHSO_2R^6$  ( $R^6$  is alkyl group), or a pharmaceutically acceptable salt thereof.

**15. (Original)** The novel indoline compound of claim 13, wherein, in the formula (I),  $R^2$  is  $-NHSO_2R^6$  [ $R^6$  is  $-NHR^7$  ( $R^7$  is hydrogen atom)], or a pharmaceutically acceptable salt thereof.

**16. (Original)** The novel indoline compound of claim 13, wherein, in the formula (I),  $R^2$  is  $-NHCONH_2$ , or a pharmaceutically acceptable salt thereof.

**17. (Original)** The novel indoline compound of claim 2, wherein the compound of the formula (I) is any of the following (1)-(5), or a pharmaceutically acceptable salt thereof:

- (1) N-(5-methanesulfonylamino-4,6-dimethyl-1-propylindolin-7-yl)-2,2-dimethylpropanamide,
- (2) N-[5-methanesulfonylamino-4,6-dimethyl-1-(2-methylpropyl)indolin-7-yl]-2,2-dimethylpropanamide,
- (3) N-(1-butyl-5-methanesulfonylamino-4,6-dimethylindolin-7-yl)-2,2-dimethylpropanamide,
- (4) N-[5-methanesulfonylamino-4,6-dimethyl-1-(3-methylbutyl)indolin-7-yl]-2,2-dimethylpropanamide,
- (5) N-(5-methanesulfonylamino-4,6-dimethyl-1-pentylindolin-7-yl)-2,2-dimethylpropanamide.

**18. (Original)** The novel indoline compound of claim 2, wherein the compound of the formula (I) is the following (1) or (2), or a pharmaceutically acceptable salt thereof:

- (1) N-(5-methanesulfonylamino-4,6-dimethyl-1-octylindolin-7-yl)-2,2-dimethylpropanamide,
- (2) N-(1-hexyl-5-methanesulfonylamino-4,6-dimethylindolin-7-yl)-2,2-dimethylpropanamide.

**19. (Original)** The novel indoline compound of claim 2, wherein the compound of the formula (I) is the following (1) or (2), or a pharmaceutically acceptable salt thereof:

- (1) N-(1-ethyl-5-methanesulfonylamino-4,6-dimethylindolin-7-yl)-2,2-dimethylpropanamide,
- (2) N-(5-methanesulfonylamino-1,4,6-trimethylindolin-7-yl)-2,2-dimethylpropanamide.

**20. (Original)** The novel indoline compound of claim 2, wherein the compound of the formula (I) is any of the following (1)-(6), or a pharmaceutically acceptable salt thereof:

- (1) N-(4,6-dimethyl-1-octyl-5-sulfamoylaminoindolin-7-yl)-2,2-dimethylpropanamide,
- (2) N-(4,6-dimethyl-1-propyl-5-sulfamoylaminoindolin-7-yl)-2,2-dimethylpropanamide,
- (3) N-(4,6-dimethyl-1-pentyl-5-sulfamoylaminoindolin-7-yl)-2,2-dimethylpropanamide,
- (4) N-[4,6-dimethyl-1-(2-methylpropyl)-5-sulfamoylaminoindolin-7-yl]-2,2-dimethylpropanamide,
- (5) N-(1-butyl-4,6-dimethyl-5-sulfamoylaminoindolin-7-yl)-2,2-dimethylpropanamide,
- (6) N-[4,6-dimethyl-1-(3-methylbutyl)-5-sulfamoylaminoindolin-7-yl]-2,2-dimethylpropanamide.

**21. (Original)** The novel indoline compound of claim 2, wherein the compound of the formula (I) is any of the following (1)-(7), or a pharmaceutically acceptable salt thereof:

- (1) N-(7-methanesulfonylamino-1,4,6-trimethylindolin-5-yl)-2,2-dimethylundecanamide,
- (2) N-(7-methanesulfonylamino-4,6-dimethylindolin-5-yl)-2,2-dimethylundecanamide,
- (3) N-[7-(2-propanesulfonylamino)-4,6-dimethylindolin-5-yl]-2,2-dimethylundecanamide,
- (4) N-[7-(2-propanesulfonylamino)-4,6-dimethylindolin-5-yl]-2,2-dimethyloctanamide,
- (5) N-[4,6-dimethyl-7-(p-toluene)sulfonylaminoindolin-5-yl]-2,2-dimethylundecanamide,
- (6) N-(4,6-dimethyl-7-sulfamoylaminoindolin-5-yl)-2,2-dimethylundecanamide,
- (7) N-(4,6-dimethyl-7-ureidoindolin-5-yl)-2,2-dimethylundecanamide.

**22. (Original)** The novel indoline compound of claim 2, wherein the compound of the formula (I) is any of the following (1)-(5), or a pharmaceutically acceptable salt thereof:

- (1) N-(4,6-dimethyl-5-nitro-1-octylindolin-7-yl)-2,2-dimethylpropanamide,
- (2) N-(5-methanesulfonylaminoethyl-4,6-dimethyl-1-octylindolin-7-yl)-2,2-dimethylpropanamide,
- (3) N-(4,6-dimethyl-1-octyl-5-ureidoindolin-7-yl)-2,2-dimethylpropanamide,
- (4) N-[5-(N-acetylsulfamoylamino)-4,6-dimethyl-1-octylindolin-7-yl]-2,2-dimethylpropanamide,
- (5) N-[5-(N-methoxycarbonylsulfamoylamino)-4,6-dimethyl-1-octylindolin-7-yl]-2,2-dimethylpropanamide.

23. (Currently amended) The novel indoline compound of claim 9 or 12, wherein, in the formula (I),  $R^2$  is  $-NHSO_2R^6$  ( $R^6$  is alkyl group), or a pharmaceutically acceptable salt thereof.

24. (Currently amended) The novel indoline compound of claim 9 or 12, wherein, in the formula (I),  $R^2$  is  $-NHSO_2R^6$  [ $R^6$  is  $-NHR^7$  ( $R^7$  is hydrogen atom)], or a pharmaceutically acceptable salt thereof.

25. (Original) The novel indoline compound of claim 2, wherein the compound of the formula (I) is any of the following (1)-(6), or a pharmaceutically acceptable salt thereof:

(1) N-(1-isopropyl-5-methanesulfonylamino-4,6-dimethylindoline-7-yl)-2,2-dimethylpropanamide,

(2) N-[1-(2,2-dimethylpropyl)-5-methanesulfonylamino-4,6-dimethylindolin-7-yl]-2,2-dimethylpropanamide,

(3) N-(1-cyclobutylmethyl-5-methanesulfonylamino-4,6-dimethylindolin-7-yl)-2,2-dimethylpropanamide,

(4) N-(1-cyclopentyl-5-methanesulfonylamino-4,6-dimethylindolin-7-yl)-2,2-dimethylpropanamide,

(5) N-(1-cyclopentyl-4,6-dimethyl-5-sulfamoylaminoindolin-7-yl)-2,2-dimethylpropanamide,

(6) N-(1-cyclopropylmethyl-5-methanesulfonylamino-4,6-dimethylindolin-7-yl)-2,2-dimethylpropanamide.

26. (Original) The novel indoline compound of claim 3, wherein the compound of the formula (I) is N-[5-methanesulfonylamino-4,6-dimethyl-1-(3-methyl-2-butenyl)indolin-7-yl]-2,2-dimethylpropanamide, or a pharmaceutically acceptable salt thereof.

27. (Original) The novel indoline compound of claim 3, wherein the compound of the formula (I) any of the following (1)-(6), or a pharmaceutically acceptable salt thereof:

- (1) N-[1-(2-ethoxyethyl)-4,6-dimethyl-5-sulfamoylaminoindolin-7-yl]-2,2-dimethylpropanamide,
- (2) N-[1-(2-ethoxyethyl)-2,4,6-trimethyl-5-sulfamoylaminoindolin-7-yl]-2,2-dimethylpropanamide,
- (3) N-[1-(2-methoxyethyl)-4,6-dimethyl-5-sulfamoylaminoindolin-7-yl]-2,2-dimethylpropanamide,
- (4) N-[1-(2-methoxyethyl)-2,4,6-trimethyl-5-sulfamoylaminoindolin-7-yl]-2,2-dimethylpropanamide,
- (5) N-[1-(2-ethylthioethyl)-4,6-dimethyl-5-sulfamoylaminoindolin-7-yl]-2,2-dimethylpropanamide hydrochloride,
- (6) N-[4,6-dimethyl-1-(2-methylthioethyl)-5-sulfamoylaminoindolin-7-yl]-2,2-dimethylpropanamide hydrochloride.

**28. (Original)** The novel indoline compound of claim 3, wherein the compound of the formula (I) is any of the following (1)-(4), or a pharmaceutically acceptable salt thereof:

- (1) N-(2-methoxymethyl-4,6-dimethyl-1-propyl-5-sulfamoylaminoindolin-7-yl)-2,2-dimethylpropanamide,
- (2) N-(2-ethoxymethyl-4,6-dimethyl-1-propyl-5-sulfamoylaminoindolin-7-yl)-2,2-dimethylpropanamide,
- (3) N-(2-methylthiomethyl-4,6-dimethyl-1-propyl-5-sulfamoylaminoindolin-7-yl)-2,2-dimethylpropanamide,
- (4) N-(2-ethylthiomethyl-4,6-dimethyl-1-propyl-5-sulfamoylaminoindolin-7-yl)-2,2-dimethylpropanamide.

**29. (Original)** The novel indoline compound of claim 3, wherein the compound of the formula (I) is the following (1) or (2), or a pharmaceutically acceptable salt thereof:

- (1) N-[1-(2-ethoxyethyl)-5-methanesulfonylamino-4,6-dimethylindolin-7-yl]-2,2-dimethylpropanamide,
- (2) N-[1-(2-methoxyethyl)-5-methanesulfonylamino-4,6-dimethylindolin-7-yl]-2,2-

dimethylpropanamide.

**30. (Currently amended)** A pharmaceutical composition comprising a novel indoline compound of ~~any of claims 1-29~~ claim 1, or a pharmaceutically acceptable salt thereof.

**31. (Currently amended)** An acyl-coenzyme A: cholesterol acyl transferase inhibitor comprising a novel indoline compound of ~~any of claims 1-29~~ claim 1, or a pharmaceutically acceptable salt thereof.

**32. (Currently amended)** A lipoperoxidation inhibitor comprising a novel indoline compound of ~~any of claims 1-29~~ claim 1, or a pharmaceutically acceptable salt thereof.

**33. (New)** The novel indoline compound of claim 12, wherein, in the formula (I),  $R^2$  is  $-NHSO_2R^6$  ( $R^6$  is alkyl group), or a pharmaceutically acceptable salt thereof.

**34. (New)** The novel indoline compound of claim 12, wherein, in the formula (I),  $R^2$  is  $-NHSO_2R^6$  [ $R^6$  is  $-NHR^7$  ( $R^7$  is hydrogen atom)], or a pharmaceutically acceptable salt thereof.

### REMARKS

The specification has been amended to reflect the national stage status. Other editorial changes have been effected to the specification which are self-explanatory.


In addition, the claims have been amended to remove the multiple dependencies to reduce the PTO filing fee and to eliminate improper multiple dependencies.

Favorable action on the merits is solicited.

Respectfully submitted,

Shouji KAMIYA et al.

By

  
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January 14, 2005